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(FILE 'HOME' ENTERED AT 14:11:15 ON 31 JUL 2001)

FILE 'HCAPLUS' ENTERED AT 14:11:25 ON 31 JUL 2001

E FERMENTATION/CT

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| | | | | |
|----|------|------------|--------|--|
| L1 | 5918 | SEA ABB=ON | PLU=ON | PURINE NUCLEOSIDE# OR NUCLEOSIDES (L) |
| | | | | PURINE OR PURINE RIBONUCLEOSIDE# |
| L2 | 373 | SEA ABB=ON | PLU=ON | L1 AND (ESCHERICHIA COLI OR E# COLI OR |
| | | | | PARACOLOBACTRUM COLIFORME) |
| L3 | 11 | SEA ABB=ON | PLU=ON | L2 AND FERMENT? |
| L4 | 7 | SEA ABB=ON | PLU=ON | L3 AND PD<19970717 |
| | | | | D IBIB AB 1-7 |
| L5 | 604 | SEA ABB=ON | PLU=ON | L1 (L) PREP/RL |
| L6 | 35 | SEA ABB=ON | PLU=ON | L5 AND (ESCHERICHIA COLI OR E# COLI OR |
| | | | | PARACOLOBACTRUM COLIFORME) |
| L7 | 20 | SEA ABB=ON | PLU=ON | L6 AND PD<19970717 |
| | | | | D IBIB AB 1-10 |
| | | | | D IBIB AB 11-20 |
| L8 | 2 | SEA ABB=ON | PLU=ON | L7 AND MUTA? |
| | | | | D IBIB AB 1-2 |

=> d ibib ab 17 1-20

L7 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:804927 HCAPLUS

DOCUMENT NUMBER: 128:75619

TITLE: Enzymic synthesis of 2',5'-dideoxy purine nucleosides and related compounds

AUTHOR(S): Fathi, Reza; Nawoschik, Kenneth J.; Zavoda, Melissa; Cook, Alan F.

CORPORATE SOURCE: PharmaGenics, Inc., Allendale, NJ, 07401, USA

SOURCE: Nucleosides Nucleotides (1997), 16(10 & 11), 1907-1920

CODEN: NUNUD5; ISSN: 0732-8311

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A wide range of 2',5'-dideoxynucleosides, including 6-substituted purine, pyrazolo[3,4-d]pyrimidine and 1-deazapurine derivs., has been enzymically prepd. using purine nucleoside phosphorylase. Specificity towards cleavage by bacterial vs. mammalian purine nucleoside phosphorylase was evaluated.

L7 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:791824 HCAPLUS

DOCUMENT NUMBER: 128:125519

TITLE: Enzymic synthesis of thymidine using bacterial whole cells and isolated purine nucleoside phosphorylase

AUTHOR(S): Pal, Suresh; Nair, Vasu

CORPORATE SOURCE: Department of Chemistry and the Center for Biocatalysis and Bioprocessing, The University of Iowa, Iowa City, IA, 52242, USA

SOURCE: Biocatal. Biotransform. (1997), 15(2), 147-158

CODEN: BOBOEQ; ISSN: 1024-2422

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:125519

AB Whole cells of *Escherichia coli* and the thermostable bacteria, *Bacillus stearothermophilus*, were used for the efficient synthesis of the biol. and industrially important compd., thymidine, using 2'-deoxyinosine and thymine as substrates. In this conversion, the 2'-deoxyribose moiety of 2'-deoxyinosine was transferred to thymine by the transdeoxyglycosylation activity of these bacterial cells. For example, in the case of *Bacillus stearothermophilus*, the yield of pure thymidine was 56% (78% conversion). When xanthine oxidase was added to this whole cell process, the product yield increased to 68% (90% conversion). In this transformation, *Bacillus stearothermophilus* was used at a temp. of 55.degree.C where the soly. of thymine is much higher than at 25.degree.C. The bacterial cells have activity over a broad pH range (approx. 4.0 to 8.0) and the yield of product varied within this pH range with the optimum pH being at 5.2. Both bacterial cells showed a sharp decrease in activity at alk. pHs. Cells of both bacteria can be used repeatedly without appreciable loss of activity. Thymidine was also produced from thymine and 2'-deoxyinosine using isolated purine nucleoside phosphorylase. A dramatic increase in conversion occurred with purine nucleoside phosphorylase in the presence of xanthine oxidase.

L7 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:758774 HCAPLUS

DOCUMENT NUMBER: 128:177464

TITLE: Cleavage effect of oligoribonucleotides substituted at the cleavage sites with modified pyrimidine- and purine-nucleosides

AUTHOR(S): Hosono, Kazumi; Gozu, Hidetaka; Hosaka, Hideo; Sakamoto, Kensaku; Yokoyama, Shigeyuki; Takai, Kazuyuki; Takaku, Hiroshi
 CORPORATE SOURCE: Narashino, Tsudanuma, Department of Industrial Chemistry, Chiba Institute of Technology, Chiba 275, Japan
 SOURCE: Biochim. Biophys. Acta (1997), 1354(3), 211-218
 CODEN: BBACAQ; ISSN: 0006-3002
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The precursor of an RNA mol. from T4-infected *E. coli* cells (p2Sp1 RNA) has the capacity to cleave itself at specific positions (UpA (139-140) and CpA (170-171)), within a putative loop and stem structure. This sequence-specific cleavage requires at least a monovalent cation and non-ionic detergents. In order to det. the influence of the pyrimidine and purine bases on these sequence-specific cleavage reactions, we studied the cleavage reactions of hairpin loop RNAs substituted at the cleavage sites with modified pyrimidine- and purine-nucleosides. The cleavage was affected by the 2'-hydroxyl groups and the bases of the pyrimidines, and the 6-amino group of the purine.

L7 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:369848 HCAPLUS
 DOCUMENT NUMBER: 125:27688
 TITLE: Gene therapy vectors and vaccines based on non-segmented negative-stranded RNA viruses
 INVENTOR(S): Wertz, Gail W.; Yu, Qingzhon; Ball, Laurence A.; Barr, John N.; Whelan, Sean P. J.
 PATENT ASSIGNEE(S): UAB Research Foundation, USA
 SOURCE: PCT Int. Appl., 70 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 9610400 | A1 | 19960411 | WO 1995-US12507 | 19950929 <-- |
| W: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5716821 | A | 19980210 | US 1994-316438 | 19940930 |
| PRIORITY APPLN. INFO.: | | | US 1994-316438 | 19940930 |

AB Recombinant methods for recovering wild-type or engineered-neg. stranded, non-segmented RNA virus genomes contg. non-coding 3' and 5' regions (e.g. leader or trailer regions) surrounding one, several or all of the genes of the virus or one or more heterologous gene(s) in the form of ribonucleocapsids contg. N, P and L proteins, which are capable of replicating and assembling with the remaining structural proteins to bud and form virions, or which are only capable of infecting one cell, or are transcribing particles, are disclosed. Novel vaccines, gene therapy vectors and antiviral compds. based on these viral particles are also disclosed.

L7 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:953788 HCAPLUS
 DOCUMENT NUMBER: 124:249856
 TITLE: 2-Chloro-2'-deoxyadenosine (cladribine) and its analogs are good substrates and potent selective inhibitors of *Escherichia coli* purine-nucleoside phosphorylase
 AUTHOR(S): Bzowska, Agnieszka; Kazimierczuk, Zygmunt
 CORPORATE SOURCE: Dep. Biophys., Univ. Warsaw, Pol.

SOURCE: Eur. J. Biochem. (1995), 233(3), 886-90

CODEN: EJBCAI; ISSN: 0014-2956

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-Chloro-2'-deoxyadenosine (CldAdo) and its analog, 2-bromo-2'-deoxyadenosine, are both effective inhibitors of the bacterial (*E. coli*) purine-nucleoside phosphorylase (PNP), with K_i values of 4.5 μ M and 6.3 μ M, resp. The examn. of a series of base-modified analogs of CldAdo showed that several other compds. have similar inhibitor properties, and that 6-benzyloxy-2-chloro-9-(2'-deoxy-.beta.-D-ribofuranosyl)purine is the most potent inhibitor with a K_i value of 0.5 μ M, competitive with respect to inosine (Ino). CldAdo itself and its base-modified analogs, discounting those substituted at C(8), are also substrates for the *E. coli* PNP and undergo rapid glycosidic bond cleavage. All compds. tested are totally inactive as substrates and inhibitors for mammalian (calf spleen) PNP and therefore constitute a new class of potent selective, although cleavable, inhibitors of bacterial phosphorylases. 8-Bromo-2-chloro-2'-deoxyadenosine and 8-thio-2-chloro-2'-deoxyadenosine are the only base-modified CldAdo derivs. showing inhibitory activity against MOLT-3 (acute T-cell leukemia) and U-937 (histiocytic lymphoma) cells and are resistant to degrdn. by *E. coli* PNO. Both analogs could be effective as oral cytotoxic agents that are noncleavable by enteric bacteria.

L7 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:572394 HCAPLUS

DOCUMENT NUMBER: 123:136872

TITLE: Complex extraction and purification of *Escherichia coli* nucleoside phosphorylase

AUTHOR(S): Bokut, S. B.; Barai, V. N.; Dudchik, N. V.; Zinchenko, A. I.

CORPORATE SOURCE: Inst. Mikrobiol., Belarus

SOURCE: Vestsi Akad. Navuk Belarusi, Ser. Biyal. Navuk (1994), (4), 45-50
CODEN: VABNE9

DOCUMENT TYPE: Journal

LANGUAGE: Belorussian

AB Dye-ligand chromatog. on Reactive Green-5-agarose and Reactive red-120-agarose was used for the purifn. of purine nucleoside phosphorylase, thymidine phosphorylase and uridine phosphorylase isolated from *Escherichia coli* BM-11 cells. Using the procedures described the enzymes were purified approx. 48-61 fold with a yield of 39-95%.

L7 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:512821 HCAPLUS

DOCUMENT NUMBER: 123:9862

TITLE: Site-selected introduction of modified purine and pyrimidine ribonucleosides into RNA by automated phosphoramidite chemistry

AUTHOR(S): Agris, P. F.; Malkiewicz, A.; Kraszewski, A.; Everett, K.; Nawrot, B.; Sochacka, E.; Jankowska, J.; Guenther, R.

CORPORATE SOURCE: Dep. Biochem., North Carolina State Univ., Chapel Hill, NC, 27695-7622, USA

SOURCE: Biochimie (1995), 77(1/2), 125-34
CODEN: BICMBE; ISSN: 0300-9084

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The study of modified nucleoside contributions to RNA chem., structure and function has been thwarted by the lack of a site-selected method of incorporation which is both versatile and adaptable to present synthetic technologies. A reproducible and versatile site-selected incorporation of

nine differently modified nucleosides into hepta- and octadecamer RNAs has been achieved with automated phosphoramidite chem. The 5'-O-(4,4'-dimethoxytrityl)-2'-O-tert-butyl dimethylsilyl-ribonucleoside-3'-O-(2-cyanoethyl-N,N-diisopropyl)phosphoramidite syntheses of m5C, D, .psi., riboT, s2U, mnm5U, m1G and m2A were designed for compatibility with the com. available major and 2'OH methylated ribonucleoside phosphoramidites. The synthesis of the m5C phosphoramidite was uniquely designed, and the first syntheses and incorporation of the two modified purine ribonucleosides are reported in detail along with that of .psi., s2U, and mnm5U. Cleavage of RNA product from the synthesis support column, deprotection of the RNA, its purifn. by HPLC and nucleoside compn. anal. are described. Modified nucleoside-contg. RNA domains were synthesized and purified in .mu.mol quantities required for biophys., as well as biochem., studies. The anticodon domain of yeast tRNA^{Phe} was synthesized with modified nucleosides introduced at the native positions: Cm32, Gm34, m1G37 (precursor to Y), .psi.39 and m5C40. The T loop and stem was synthesized with riboT54 and the D loop and stem with D16 and D17. The *E. coli* tRNA^{Glu2} anticodon domain was synthesized with mnm5U at wobble position 34, but an attempt at incorporating s2U at the same position failed. The unprotected thio group was labile to the oxidn. step of the cyclical process. Chem. synthesized anticodon and T domains have been used in assays of tRNA structure and function (Guenther et al (1994) *Biochimie* 76, 1143-1151).

L7 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:88825 HCAPLUS

DOCUMENT NUMBER: 122:23207

TITLE: Purine nucleoside phosphorylase: inhibition by purine N(7)- and N(9)-acyclonucleosides; and substrate properties of 7-.beta.-D-ribofuranosylguanine and 7-.beta.-D-ribofuranosylhypoxanthine

AUTHOR(S): Bzowska, A.; Ananiev, A. V.; Ramzaeva, N.; Alksins, E.; Maurins, J. A.; Kulikowska, E.; Shugar, D.

CORPORATE SOURCE: Inst. Exptl. Phys., Univ. Warsaw, Warsaw, 02-089, Pol.

SOURCE: *Biochem. Pharmacol.* (1994), 48(5), 937-47

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 10 N(7)- and N(9)-acyclonucleosides of guanine and 8-substituted guanines (8-Br, 8-SH and 8-NH₂); and two N(7)-acyclonucleosides of hypoxanthine, were tested for their ability to inhibit purine nucleoside phosphorylase (PNP) (E.C. 2.4.2.1) from human erythrocytes and rabbit kidney. The acyclic chains contained a nitrogen in place of a carbon at the 3', 4' or 5' position and, in one case, an ether oxygen at the 2' position. Most striking was the finding that one of the N(7)-acyclonucleoside analogs, 7-[(1,3-dihydroxypropyl-2)amino]ethylguanine, proved to be a 3-fold more effective inhibitor than its corresponding N(9) counterpart, with $K_i = 5$ vs 14 .mu.M for the human enzyme and 0.7 vs 2.3 .mu.M for the rabbit enzyme. Both analogs, as well as the others examd., inhibited phosphorolysis competitively with respect to nucleoside substrates (inosine with the human enzyme and guanosine with the rabbit enzyme). The foregoing logically led to the finding that the 7-.beta.-D-ribosides of guanine (N7Guo) and hypoxanthine (N7Ino) were weak substrates of PNP from human erythrocytes, calf spleen and *E. coli*. With the human enzyme the pseudo-first-order rate consts. (v_{max}/K_m) for phosphorolysis of N7Guo and N7Ino were 0.08 and 0.02% that for Ino. The Michaelis consts. (K_m) for N7Guo were 27 (calf PNP), 108 (human PNP) and 450 .mu.M (*E. coli* PNP). For N7Ino the corresponding K_m values were 1.52, 1.26 and 0.64 mM. Four previously well-characterized N(9)-acyclonucleoside inhibitors of calf spleen PNP were found to inhibit phosphorolysis of N7Ino by the same enzyme 2-10-fold more effectively than the parent Ino. The overall results, along with the known excellent substrate properties of N(7)-alkyl- Guo and Ino (Browska et al. *J. Biol. Chem.* 263, 9212-9217, 1988), were examd. in relation to

present concepts regarding binding of substrates and inhibitors at the active site(s) of these enzymes.

L7 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:621999 HCAPLUS

DOCUMENT NUMBER: 121:221999

TITLE: Preparation of adenosine kinase-inhibiting purine nucleoside analogs as antiinflammatory agents

INVENTOR(S): Firestein, Gary Steven; Ugarkar, Bheemarao Ganapatrao; Miller, Leonard Paul; Gruber, Harry Edward; Bullough, David Andrew; Erion, Mark David; Castellino, Angelo John

PATENT ASSIGNEE(S): Gensia, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|--------------|
| WO 9417803 | A1 | 19940818 | WO 1994-US1340 | 19940203 <-- |
| W: | AT, AU, BB, BG, BR, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ | | | |
| RW: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9462365 | A1 | 19940829 | AU 1994-62365 | 19940203 <-- |
| EP 682519 | A1 | 19951122 | EP 1994-909558 | 19940203 <-- |
| R: | CH, DE, FR, GB, IT, LI | | | |
| US 5646128 | A | 19970708 | US 1994-349125 | 19941201 <-- |
| PRIORITY APPLN. INFO.: | | | US 1993-14190 | A 19930203 |
| | | | US 1989-408707 | B2 19890915 |
| | | | US 1990-466979 | B2 19900118 |
| | | | US 1991-647117 | B2 19910123 |
| | | | US 1991-812916 | B2 19911223 |
| | | | US 1994-192645 | B1 19940203 |
| | | | WO 1994-US1340 | W 19940203 |

OTHER SOURCE(S): MARPAT 121:221999

AB Novel nucleosides I [A = O, CH₂, S; B' = (CH₂)_nB, alkenyl, alkynyl; B = H, alkyl, alkoxy, NH₂, alkylamino, etc.; C₁, C₂ = H, acyl, hydrocarbyloxycarbonyl, or C₁C₂ = C(:O), .alpha.-alkoxyalkylidene; X = CD; D = H, halo, alkyl, cyano, CO₂H, etc.; Y = N, CE; E = H, halo, alkyl, alkylthio; F = alkyl, aryl, halo, cyano, indolyl, pyrrolidinyl, etc.; G = H, halo, alkyl, alkoxy, alkylamino, alkylthio; n = 1-4], prepd. by multistep procedures which are described, selectively inhibit adenosine kinase and are useful in treatment of conditions characterized by an inflammatory response. Such conditions include sepsis, arthritis, autoimmune disease, burns, psoriasis, conjunctivitis, etc. Thus, mice with endotoxemia resulting from injection of **Escherichia coli** lipopolysaccharide showed a dose-dependent increase in survival in response to i.v. injection of the adenosine kinase inhibitor, 4-amino-1-(5-amino-5-deoxy-1-.beta.-D-ribofuranosyl)-3-bromopyrazolo[3,4-d]pyrimidine-HCl; this effect was antagonized by the adenosine receptor antagonist 8-(p-sulfophenyl)theophylline.

L7 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:186327 HCAPLUS

DOCUMENT NUMBER: 116:186327

TITLE: Relaxation-matrix analysis of the transferred nuclear Overhauser effect for finite exchange rates

AUTHOR(S): London, Robert E.; Perlman, Michael E.; Davis, Donald G.

CORPORATE SOURCE: Lab. Mol. Biophys., Natl. Inst. Environ. Health Sci.,
Research Triangle Park, NC, 27709, USA
SOURCE: J. Magn. Reson. (1992), 97(1), 79-98
CODEN: JOMRA4; ISSN: 0022-2364

DOCUMENT TYPE: Journal
LANGUAGE: English

AB A matrix formalism is developed for calcns. of time-dependent nuclear Overhauser effects in systems undergoing chem. exchange, and the anal. is applied to the interpretation of data obtained in transferred-NOE expts. Simulations have been performed for a wide variety of nuclear geometries, and preliminary data for the reversible binding of the inhibitor tubercidin to bacterial purine nucleoside phosphorylase have also been obtained. Although theor. the initial buildup rate of the NOE interaction is independent of the exchange-rate const. k , this independence persists for such a short period of time that it is exptl. unobservable unless the exchange rate is extremely high. For the parameters used in the models, calcd. buildup rates corresponding to mixing times of 10-100 ms exhibit a strong dependence on k . Of greatest interest is the observation that a lag in the development of the transferred NOE, generally believed to characterize indirect relaxation pathways, frequently is observable only at very high rates of chem. exchange and is so minimal as to be exptl. undetectable. Alternatively, a pronounced lag phase is predicted if the exchange rate is sufficiently slow that the obsd. NOE corresponds to only the free species. An apparent lag can also be predicted to result from the small neg. NOEs of the uncomplexed species for some exchange parameters. The anal. has also been extended to include macromol. (enzyme) protons, and several models for the effects of enzyme-mediated relaxation have been evaluated. These calcns., combined with the limited ability of the researcher to control most of the parameters involved in this type of study, suggest significant problems with interpretations based on initial rate measurements and strongly support the need for an independent detn. of the rate of chem. exchange and for the use of model calcns. such as those presented here in the interpretation of transferred-NOE studies.

L7 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:630517 HCAPLUS
DOCUMENT NUMBER: 115:230517
TITLE: 2',3'-Dideoxypruine nucleoside virucides microbial
manufacture
INVENTOR(S): Kojima, Eiji; Ishida, Shuji; Yoshioka, Hidetoshi;
Murakami, Kunimutsu
PATENT ASSIGNEE(S): Sanyo-Kokusaku Pulp Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|--------------|
| | ----- | ---- | ----- | ----- | ----- |
| | JP 03047086 | A2 | 19910228 | JP 1989-181885 | 19890714 <-- |
| AB | 2',3'-Dideoxypurine nucleosides (Markush structure given) are manufd. from purine analogs (Markush structure given) and 2',3'-dideoxycytidine or 2',3'-dideoxyuridine or 3'-deoxythymidine in the presence of phosphates with an immobilized microorganism, e.g. <i>Escherichia coli</i> . The method can be used from com. prepn. of 2',3'-dideoxypurine nucleotides; the cost is low; the immobilized microorganism can be easily regenerated; and the products can be easily recovered. E. coli JA-300 was immobilized on .kappa.-carrageenan by a known method to obtain beads of immobilized E. coli JA-300. Prepn. of 2',3'-dideoxypurine nucleosides from 2'-3'-dideoxyuridine and various purine analogs using the immobilized E. coli | | | | |

JA-300 at 45.degree. with agitation was shown. The yield was 27-70%.

L7 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:102707 HCAPLUS

DOCUMENT NUMBER: 114:102707

TITLE: Preparation of 2',3'-dideoxy purine nucleosides by microbial transglycosidation and their use as antiviral agents and in genetic engineering

INVENTOR(S): Kojima, Eiji; Yoshioka, Hidetoshi; Fukinbara, Hidenori; Murakami, Kunichika

PATENT ASSIGNEE(S): Sanyo-Kokusaku Pulp Co., Ltd., Japan

SOURCE: Brit. UK Pat. Appl., 41 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|--------------|
| GB 2228479 | A1 | 19900829 | GB 1989-18417 | 19890811 <-- |
| GB 2228479 | B2 | 19931020 | | |
| JP 02308797 | A2 | 19901221 | JP 1989-46183 | 19890227 <-- |
| CA 1338532 | A1 | 19960820 | CA 1989-607104 | 19890731 <-- |
| US 5053499 | A | 19911001 | US 1989-388806 | 19890803 <-- |
| FR 2643558 | A1 | 19900831 | FR 1989-11884 | 19890912 <-- |
| FR 2643558 | B1 | 19940211 | | |
| DE 4004558 | A1 | 19900927 | DE 1990-4004558 | 19900214 <-- |
| DE 4004558 | C2 | 19980212 | | |
| US 5563049 | A | 19961008 | US 1995-405395 | 19950315 <-- |

PRIORITY APPLN. INFO.: JP 1989-46183 19890227
US 1989-388806 19890803
US 1991-726403 19910705
US 1992-980445 19921123

OTHER SOURCE(S): MARPAT 114:102707

AB The title nucleosides (I, II; R = Q; X, Y = N, CH; R1 - R5 = H, OH, NH2, alkyl, halo, alkoxy, SH), particularly useful as antiretroviral agents for prevention and treatment of AIDS (no data), are prepd. by reacting purines and azapurines (I, II; R = H, ribofuranosyl, deoxyribofuranosyl) with 2',3'-dideoxycytidine, 2',3'-dideoxyuridine, or 3'-deoxythymidine in aq. soln. in the presence of phosphate through the action of microorganisms of the Escherichia, Klebsiella, or Erwinia genus. Thus, 7.0 mmol 2',3'-dideoxyuridine and 7.0 mmol purine was stirred 4 h at 50.degree. with a suspension of *E. coli* (prepn. given) in phosphate buffer (pH 7.5) to give, after removal of the bacterium bodies and chromatog. on a HP-20 (Mitsubishi Kasei) and silica gel column, 43% 9-.beta.-D-2',3'-dideoxyribofuranosylpurine.

L7 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:24477 HCAPLUS

DOCUMENT NUMBER: 114:24477

TITLE: 9-(Difluorophosphonoalkyl)guanines as a new class of multisubstrate analog inhibitors of purine nucleoside phosphorylase

AUTHOR(S): Halazy, S.; Ehrhard, A.; Danzin, Charles

CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, F-67009, Fr.

SOURCE: J. Am. Chem. Soc. (1991), 113(1), 315-17

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 9-(5,5-Difluoro-5-phosphonopentyl)guanine (I) was synthesized as a potential multisubstrate analog inhibitor of purine nucleoside phosphorylase (EC 2.4.2.1, PNP). At pH 7.4, I has a Ki value 18-, 26-, 25-, and 5.5-fold lower than that of the nonfluorinated analog

9-(5-phosphonopentyl)guanine (II) regarding PNP from human erythrocyte, rat erythrocyte, calf spleen, and *Escherichia coli*, resp. Further studies with human erythrocytic PNP show that at pH 6.2 the difference in K_i value is more pronounced (K_{i2}/K_{i3} is 96), and at pH 8.8, where II and I are both essentially present in the unprotonated form, the ratio is 8. The superiority of the difluorophosphonate I over the phosphonate II is explained by electronic as well as by steric effects.

L7 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:493725 HCAPLUS
 DOCUMENT NUMBER: 113:93725
 TITLE: Purine nucleoside phosphorylase: purification using an ether-linked formycin B/Sepharose 6B resin with unusual properties
 AUTHOR(S): Hall, Willard W.; Krenitsky, Thomas A.
 CORPORATE SOURCE: Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
 SOURCE: Prep. Biochem. (1990), 20(1), 75-85
 CODEN: PRBCBQ; ISSN: 0032-7484
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Formycin B [9-deazainosine] was reacted with epoxy-activated Sepharose 6B to form an affinity resin for purine nucleoside phosphorylase (PNPase). This resin had a large capacity (7600 units/mL) for the enzyme from *Escherichia coli*. Enzyme retention was dependent on high ionic strength. Although this property was reminiscent of hydrophobic interaction chromatog., analogous resins prepd. with pseudouridine or monoethanolamine instead of with formycin B did not retain the enzyme even at high ionic strength. Furthermore, hypoxanthine facilitated elution of the enzyme from the resin. It appeared, therefore, that the enzyme was not bound simply by hydrophobic interactions. A simple 2-step purifn. procedure for PNPase from *E. coli* was devised using this resin. The overall recovery was 50%, and the purity of the final prepn. was >95%. This resin was also useful in the purifn. of PNPase from human erythrocytes. The ether linkage between formycin B and Sepharose 6B, together with the C-C linkage between the pentose and heterocyclic moieties of formycin B, provided stability to both chem. and enzymic degrdn. After 5 yr of use and exposure to a variety of biol. prepn., the resin showed no detectable decrease in its ability to bind PNPase.

L7 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1982:91647 HCAPLUS
 DOCUMENT NUMBER: 96:91647
 TITLE: Deazapurine nucleosides and their formulations
 INVENTOR(S): Rideout, Janet Litster; Krenitsky, Thomas Anthony
 PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
 SOURCE: Eur. Pat. Appl., 34 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------|------|----------|-----------------|--------------|
| EP 38569 | A2 | 19811028 | EP 1981-103045 | 19810422 <-- |
| EP 38569 | A3 | 19811209 | | |
| EP 38569 | B1 | 19850130 | | |
| R: BE, CH, DE, FR, GB, NL, SE | | | | |
| DK 8101800 | A | 19811024 | DK 1981-1800 | 19810422 <-- |
| DK 149958 | B | 19861103 | | |
| DK 149958 | C | 19870427 | | |
| JP 56166199 | A2 | 19811221 | JP 1981-61116 | 19810422 <-- |

CA 1168608 A1 19840605 CA 1981-375895 19810422 <--
 PRIORITY APPLN. INFO.: GB 1980-13410 19800423
 AB 4-amino-1-(2-deoxy-.beta.-D-ribofuransoyl)-1H-imidazo[4,5-c]pyridine (I) [78582-17-9] or its org. esters of salts are prepd. and used as inflammation inhibitors in oral, parenteral, rectal of topical formulations. Thus, a reaction mixt. consisted of an aq. suspension (26.9 mL) of 4-amino-1H-imidazo[4,5-c]pyridine-2HCl [80639-85-6] 2.4, 2-deoxythymidine [50-89-5] 7.2, K2HPO4 2.7, KN3 0.13 mM, **E. coli** purine nucleoside phosphorylase [9030-21-1] 1120 and **E. coli** thymidine phosphorylase [9030-23-3] 3750 IU. The pH was maintained at 6.7, and after 6 days at 37.degree., the reaction mixt. was filtered, centrifuged and the supernatant passed through a Sephadex G-10 column and eluted with H2O. Fractions contg. the product were rechromatographed over a Dowex-1 hydroxide column. The fractions contg. the product were dried and yielded 0.017 g I. Tablets were prepd. contg. 100 mg I. The immunosuppressive and the antiinflammatory activities of I were demonstrated in vitro and on lab. animals, resp.

L7 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1981:420740 HCAPLUS
 DOCUMENT NUMBER: 95:20740
 TITLE: Purine nucleoside synthesis: an efficient method employing nucleoside phosphorylases
 AUTHOR(S): Krenitsky, Thomas A.; Koszalka, George W.; Tuttle, Joel V.
 CORPORATE SOURCE: Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
 SOURCE: Biochemistry (1981), 20(12), 3615-21
 CODEN: BICHAW; ISSN: 0006-2960
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB An improved method for the enzymic synthesis of purine nucleosides is described. Pyrimidine nucleosides were used as pentosyl donors and 2 phosphorylases were used as catalysts. One of the enzymes, either uridine phosphorylase (I) or thymidine phosphorylase (II), catalyzed the phosphorolysis of the pentosyl donor. The other enzyme, purine nucleoside phosphorylase (III), catalyzed the synthesis of the product nucleoside by utilizing the pentose 1-phosphate ester generated from the phosphorolysis of the pyrimidine nucleoside. I, II, and III were sepd. from each other in exts. of **Escherichia coli** by titrn. with Ca phosphate gel. Each enzyme was further purified by ion-exchange chromatog. Factors that affect the stability of these catalysts were studied. The pH optima for the stability of I, II, and III were 7.6, 6.5, and 7.4, resp. The order of relative heat stability was I > III > II. The stability of each enzyme increased with increasing enzyme concn. This dependence was strongest with II and weakest with I. Of the substrates tested, the most potent stabilizers of I, II, and III were uridine, 2'-deoxyribose 1-phosphate, and ribose 1-phosphate, resp. Some general guidelines for optimization of yields are given. In a model reaction, optimal product formation was obtained at low phosphate concns. As examples of the efficiency of the method, the 2'-deoxyribonucleoside of 6-(dimethylamino)purine and the ribonucleoside of 2-amino-6-chloropurine were prepd. in yields of 81 and 76%, resp.

L7 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1980:2839 HCAPLUS
 DOCUMENT NUMBER: 92:2839
 TITLE: Enzymatic synthesis of purine arabinonucleosides
 INVENTOR(S): Krenitsky, Thomas Anthony; Elion, Gertrude Belle; Rideout, Janet Elizabeth
 PATENT ASSIGNEE(S): Wellcome Foundation Ltd., Engl.
 SOURCE: Eur. Pat. Appl., 25 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------|------|----------|-----------------|--------------|
| EP 2192 | A1 | 19790613 | EP 1978-101295 | 19781102 <-- |
| EP 2192 | B1 | 19811104 | | |
| R: CH, DE, FR, GB | | | | |
| GB 1573777 | A | 19800828 | GB 1977-45668 | 19771103 <-- |
| JP 54095794 | A2 | 19790728 | JP 1978-134618 | 19781102 <-- |

PRIORITY APPLN. INFO.: GB 1977-45668 19771103

AB Purine 9.beta.-D-arabinonucleosides, compds. useful as antivirals, are synthesized by reacting a purine base with arabinose-1-phosphate generated enzymically from an arabinosyl donor and inorg. phosphate. The enzyme system consists of uridine phosphorylase (I) and purine nucleoside phosphorylase (II) and the detn. and purifn. of the 2 enzymes from *Escherichia coli* is described. Thus, the reaction mixt. consists of an aq. suspension (1 L) contg. 57 mmol uracil arabinonucleoside, 118 mmol 2,6-diaminopurine, 3 mmol K₂HPO₄, 3 mmol NaN₃, 15,000 units of II, and 8000 units of I. The mixt. was adjusted to pH 7.1 before addn. of the enzymes. After 7 days at 37.degree., the insol. material was collected, suspended in anhyd. MeOH (1.8 L), and boiled for 1 h. The residue was resuspended and boiled in 350 mL MeOH. The filtrate was then lyophilized and returned to the supernatant fluid of the original reaction mixt. Addnl. uracil arabinonucleoside (44 mmol) was added and, after 5 days at 37.degree., the insol. material in the reaction mixt. was extd. as described above. The overall yield of 2,6-diamino-9.beta.-D-arabinofuranosylpurine (60.7 mmol) was 51% with respect to the amt. of free base used and 60% with respect to the amt. of uracil arabinonucleoside used.

L7 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1977:485195 HCAPLUS

DOCUMENT NUMBER: 87:85195

TITLE: Synthesis and biological properties of
p-[bis(2-chloroethyl)amino]-benzaldehyde
9-.beta.-D-ribofuranosylpurin-6-ylhydrazone

AUTHOR(S): Fleysner, M. H.; Bloch, A.

CORPORATE SOURCE: Grace Cancer Drug Cent., Roswell Park Mem. Inst.,
Buffalo, N. Y., USA

SOURCE: J. Carbohydr., Nucleosides, Nucleotides (1977
) , 4(2), 121-7
CODEN: JCNNAF

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The title compd. I was prepd. in 71% yield by condensation of
6-hydrazino-6-(.beta.-D-ribofuranosyl)purine with p-(ClCH₂CH₂)₂NC₆H₄CHO at
room temp. in DMF in the presence of mol. sieves. I inhibited in vitro
growth of *E. coli*, mammary carcinoma TA-3, taper
heptoma, and leukemia L-1210 cells by 50% at 10⁻⁶ to 10⁻⁷ molar concn.
This activity was 3-5 times greater than that of the known aglycone.

L7 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1970:404139 HCAPLUS

DOCUMENT NUMBER: 73:4139

TITLE: Preparation and activity of the 4'-thio-derivatives of
some 6-substituted purines nucleosides

AUTHOR(S): Bobek, Miroslav; Whistler, Roy L.; Bloch, Alexander
CORPORATE SOURCE: Dep. of Biochem., Purdue Univ., Lafayette, Indiana,
USA

SOURCE: J. Med. Chem. (1970), 13(3), 411-13
CODEN: JMCMAR

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 6-Chloro-9-(4-thio-.beta.-D-ribofuranosyl)purine was prepd. by condensation of 2,3,5-tri-O-acetyl-4-thio-D-ribofuranosyl chloride with the chloromercuri deriv. of 6-chloropurine, followed by ammonolysis. Nucleophilic substitution was used to replace the 6-chloro with NH₂, Me₂N, or SH, and dehalogenation furnished the 4'-thio analog of 9-.beta.-D-ribofuranosylpurine (nebularine). Replacement of the O in the carbohydrate skeleton with S led to marked changes in the potency of the compds., as detd. in vitro with *Streptococcus faecium*, *Escherichia coli*, Leukemia L-1210, and Ehrlich ascites cells. Depending on the test system used, the potency of the thioribosyl nucleotides was greater or smaller than that of the corresponding ribosyl analog. These difference in activity are likely related to differences in the metabolic disposition of the compds. For example, unlike 6-mercapto-9-(.beta.-D-ribofuranosyl)purine, the corresponding thio-D-ribosyl analog did not undergo enzymic cleavage of its glycosyl bond. As a result, a mutant strain of *S. faecium* resistant to the inhibitory effect of 6-mercapto-9-(4-thio-.beta.-D-ribofuranosyl)purine, was still sensitive to the action of both 6-mercaptapurine and 6-mercapto-9-(.beta.-D-ribofuranosyl)purine. When used in combination with the corresponding ribosyl analogs, the thioribosyl derivs. tested interfered with the growth of *S. faecium* in a synergistic manner. In view of this synergism and the obsd. activity against resistant strains, these compds. deserve evaluation in vivo.

L7 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1970:3706 HCAPLUS

DOCUMENT NUMBER: 72:3706

TITLE: Synthesis and biological activity of some new N6-substituted purine nucleosides

AUTHOR(S): Fleysher, Maurice H.; Bloch, A.; Hakala, M. T.; Nichol, C. A.

CORPORATE SOURCE: Roswell Park Mem. Inst., Buffalo, N. Y., USA

SOURCE: J. Med. Chem. (1969), 12(5), 1056-61

CODEN: JMCMAR

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of N6-2-phenoxyethyl-, N6-benzyl-, N6-n-hexyl-, N6-n-pentyl-, N6-phenyl-, N6-2-thienyl-, and N6-2-ethoxyethyl-adenosines was carried out by quaternization of the N1 of adenosine with the appropriate halide, followed by rearrangement to the product in aqueous NH₃, or by nucleophilic substitution of 6-chloro-9-D-ribofuranosylpurine with the appropriate amine. Also synthesized were the N6-(.DELTA.2-isopentenyl) and N6-allyl derivs. of the antibiotic tubercidin (7-deazaadenosine). The compds. were examd. for biol. activity in a no. of test systems. All of the adenosine derivs. examd. showed cytotoxic activity in the tobacco with bioassay. Similarly, at low concns. (10⁻⁸ to 10⁻⁶M), the N6-substituted adenosines tested, stimulated the growth of a human leukemic cell line (6410). At higher concns., they decreased the viability of this line of leukemia myeloblasts of line HRIK of Burkitt's lymphoma, and line LKID of leukemic lymphoblasts, whereas they were all ineffective against a culture of normal leukocytes. The N6-substituted tubercidins on the other hand inhibited the normal leukocytes, but were variably effective against the tumor lines. Most of the compds. interfered with the growth of *Escherichia coli* and some with the growth of Sarcoma 180 cells in vitro. A moderate but significant increase in survival time of mice bearing leukemia L1210 was produced by four of the adenosine derivatives.